NEUROSCIENCE DISCIPLINE SCIENCE PLAN
TABLE OF CONTENTS

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1.0 INTRODUCTION

Over the past two decades, NASA's efforts in the neurosciences have developed into a program of research directed at understanding the acute changes that occur in the neurovestibular and sensorimotor systems during short-duration space missions. However, the proposed extended-duration flights of up to 28 days on the Shuttle orbiter and 6 months on Space Station Freedom, a lunar outpost, and Mars missions of perhaps 1-3 years in space, make it imperative that NASA's Life Sciences Division begin to concentrate research in the neurosciences on the chronic effects of exposure to microgravity on the nervous system. Major areas of research will be directed at understanding (1) central processing, (2) motor systems, (3) cognitive/spatial orientation, and (4) sensory receptors.

1.1 PURPOSE

The purpose of this Discipline Science Plan is to provide a conceptual strategy for NASA's Life Sciences Division research and development activities in the comprehensive area of neurosciences. It covers the significant research areas critical to NASA's programmatic requirements for the Extended-Duration Orbiter, Space Station Freedom, and exploration mission science activities. These science activities include ground-based and flight; basic, applied, and operational; and animal and human research and development. This document summarizes the current status of the program, outlines available knowledge, establishes goals and objectives, identifies science priorities, and defines critical questions in the subdiscipline areas of nervous system function. It contains a general plan that will be used by NASA Headquarters Program Offices and the field centers to review and plan basic, applied, and operational intramural and extramural research and development activities in this area.

1.2 BRIEF DESCRIPTION OF THE DISCIPLINE

Neuroscience is a biological discipline whose goals are to describe and understand how the brain controls behavior. Behavior controlled by the brain ranges from

- the regulation of hormonal secretions that control basic body functions as varied as physiological and emotional responses to stress and the regulation of blood pressure
- to simple reflexive controls, such as spinal and brainstem reflexes, which provide automatic behavioral responses to a variety of environmental stimuli
- to the performance of complex sensorimotor behavioral tasks, such as locomotion, posture, or the eye-hand-head coordination required to pilot an aircraft or a spacecraft

- to the perception of the body's orientation in space
- to the control of learning and memory.

Information from sensors of light, sound, blood pressure, muscle length, and acceleration, among others, are evaluated by the brain to produce reactions to environmental conditions that are appropriate for the survival of the organism. NASA's Neuroscience Program should be an attempt to understand how the brain controls responses to the special environmental conditions of space travel, such as weightlessness, fractional gravity, unusual combinations of acceleration, radiation, and the stress induced by long confinement in dangerous, close quarters.

2.0 BACKGROUND

2.1 BRIEF HISTORY OF THE DISCIPLINE AS PART OF SPACE LIFE SCIENCES

During the early years of NASA's manned space flight program, efforts in the life sciences were driven by operational medicine and biomedical support of short-duration missions such as the Mercury and Gemini flight series. During these missions, no significant problems arose with regard to sensory system function. However, during the Apollo missions, a number of astronauts reported mild to severe motion sickness symptoms and, in the early 1970's, NASA initiated studies directed at understanding the basic etiology of space motion sickness. In addition, studies were undertaken to develop tests that would predict susceptibility and enhance development of suitable countermeasures.

Over the past two decades, NASA's efforts in the neurosciences developed into a program of extensive research directed at understanding neurovestibular and sensorimotor system function, particularly as these functions relate to space motion sickness. Despite these efforts, space motion sickness remains a significant and unpredictable problem during the first few days of space flight. One of the major difficulties in understanding the etiology of space motion sickness has been a lack of understanding of its neuroanatomical and physiological substrates. More recently, it has been realized that attention must be devoted to other anatomical, neurophysiological, and perceptual changes that occur during the process of adaptation to altered gravity, and that may have implications for readaption on return to a gravitational environment.

2.2 CURRENT KNOWLEDGE

Current knowledge about physiological changes associated with short-term and long-term space flight is summarized in Appendix I, which is from Space Physiology and Medicine, 2nd. edition by Drs. Nicogossian, Leach-Huntoon, and Pool.

2.2.1 Introduction

A number of important nervous system functions are affected by space flight. Among them are spatial orientation, posture, vestibular reflexes, central nervous system processing, and autonomic control. All have received attention in ground-based studies, but most are incompletely understood in space flight.

2.2.2 Spatial Orientation

Spatial orientation is the relationship between a body-oriented coordinate system and external reference frames. It results from the integration of auditory, visual, vestibular, tactile and proprioceptive signals, and from a comparison between them and the motor-command or efference-copy signals arising in the brain.

Cues that determine spatial orientation vary in the initial phases of adaptation to weightlessness. Some individuals become strongly dependent on vision as a substitute for the absence of gravity, orienting themselves with respect to familiar vertical references. Others are more "body oriented" and align their sense of the vertical along their long body axis. These people do not become as disoriented when working in unusual attitudes relative to their external environment or during motion where visual cues for vertical orientation are absent. Postflight alterations of spatial orientation include illusions such as a sense of disorientation when making pitching or rolling movements, changes in linear acceleration thresholds, and unusually strong visual influences on orientation. In addition, at re-entry and shortly thereafter, tilting motions of the head may cause a sense of sudden linear translation in the opposite direction.

2.2.3 Posture

Posture is altered to meet the mechanical demands of space. Elimination of the need for antigravity postures in microgravity creates a unique context for reinterpretation of sensory inputs and coordination of muscular actions. Studies of postural system adaptation to microgravity are limited, but indicate that there are changes in the interpretation of sensory inputs and in the coordination of muscular actions. Voluntary pointing accuracy and perception of static limb position are impaired in microgravity, and naive subjects, when asked to orient themselves vertically in relation to visual surroundings and support surfaces, assume skewed postures. The H reflex, reflecting supraspinal and otolithic control of motoneurons, appears to be depressed in flight and enhanced for several days postflight. Returning crewmembers experience difficulties walking and standing with their eyes closed, and in making quick turns. These symptoms occur even after missions of relatively short duration, where changes in muscular strength are limited. Thus, they cannot be ascribed to skeletal muscle changes, but to adaptation of central motor programs to microgravity.

2.2.4 Vestibulo-Ocular Reflexes

The vestibulo-ocular reflex (VOR) provides ocular compensation to stabilize gaze so that clear vision can be maintained during head movements. Both semicircular canals and otoliths control eye movements. The canals sense angular or turning head

movements. The otolith organs sense translation (linear head movements) and also respond to gravity. Only the response to gravity is lost in space flight. Therefore, ocular reactions, which are dependent on the otoliths and on the processing of otolith information, are especially likely to be affected by exposure to microgravity. There have been some experiments, both American and Soviet, that indicate that changes in the VOR and alterations in optokinetic reflexes occur during space flight. However, insufficient data are available to know exactly how VORs change, or what the significance of their changes is to behavior and performance.

2.2.5 Processing in the Vestibular System

The characteristics of the neural input from the inner ear, as well as from the skin, tendons, joint afferents, and gastrointestinal receptors, which forms the physiological basis for alterations in function in weightlessness, remain unknown. There is also little information about how central neurons in the brainstem or cerebellum respond to altered input during exposure to microgravity.

2.2.6 Space Motion Sickness

Numerous reports have summarized the information currently available on space motion sickness, e.g. "Research Opportunities in Space Motion Sickness," edited by J. M. Talbot (NASA Contractor Report 3708, July 1983). This report stated:

> Development of a widely accepted, scientific definition of space sickness is hampered by a serious lack of data on the precise causal stimulus or stimuli and on the basic biologic mechanisms involved in the genesis of and habituation to, the disorder. . . The most popular theories include sensory mismatch, sensory conflict, and sensory overstimulation and overflow. While these theories appear basically logical, they fail to identify the precise, adequate stimulus for space sickness. . .with the exception of drugs, promising approaches toward prevention and control of space sickness have not led to practical countermeasures; for example, means of identifying resistant individuals and vestibular adaptation training.

There is a low correlation between results from ground-based tests and those performed in microgravity. Of considerable interest is the fact that astronauts were highly resistant to the adverse effect of cross-coupled angular accelerations after they had adapted to the absence of the Earth's gravitational force during Skylab missions. Thresholds for induction of motion sickness were elevated in these subjects for up to 1 week postflight, indicating that sensory adaptation to space had been responsible for their decreased susceptibility to Coriolis stimulation.

As the number of astronauts flying multiple missions has increased, it has become evident that those who have flown previously appear to be less susceptible to space motion sickness. It is not known if this decreased susceptibility is due to a change in strategy in controlling head and body movements or to more rapid central adaptation during subsequent exposures.

At the present time, the only measures being used by NASA to counter space motion sickness are prophylactic and therapeutic anti-motion sickness drugs. Some of these compounds, such as scopolamine and dexedrine, have direct effects on both the vestibular and visual oculomotor systems and interfere with normal sleep mechanisms, although in recent trials parenteral phenergan has appeared to be more effective, with fewer side effects. Nevertheless, since some astronauts require 2 to 4 days to overcome motion sickness symptoms, productivity on short-duration Shuttle flights (3 to 10 days) is often compromised. Should an emergency extravehicular activity (EVA) be required during the early portion of the flight, space motion sickness could pose a serious health and operational hazard. NASA's Life Sciences Division is in the process of validating a number of preflight adaptation devices that may prove effective in preadapting astronauts to the visual-vestibular stimulus conflict that occurs in microgravity. It is hypothesized that this type of preflight training will decrease the incidence of space motion sickness.

3.0 DISCIPLINE GOALS, OBJECTIVES, AND CRITICAL QUESTIONS

The overall goals of NASA's Neuroscience Program are to

- Understand the acute and long-term central and peripheral nervous system adaptation to space
- Develop adequate physiological and performance countermeasures.

Determining how the organism readapts to gravitational environments will also become a major goal as NASA commits to longer duration missions. The critical questions will differ, depending on the duration of the mission and whether the effect is medium or long-term. It is taken as a given that understanding the effects of microgravity on the human organism is predicated on an understanding of normal physiological functioning in a 1-g environment. Therefore, it is worthwhile to conduct ground-based studies of the relevant central and peripheral systems that are compromised by exposure to microgravity.

Over the past 20 years, numerous reports have been published related to NASA's requirements for the neuroscience research. These reports have typically stressed major goals and overall objectives relative to the neurosciences and space flight. Of necessity they have been very broad. This plan incorporates recommendations from reports by the Committee on Space Biology and Medicine (Goldberg), the NASA Life Sciences Strategic Planning Study Committee (Robbins), and the Federation of American Societies for Experimental Biology (FASEB) (see 6.0, Selected References). Its purpose is to identify critical questions in the neurosciences that are specific and that lead to experimental solutions.

The sections that follow identify the major objectives of NASA's research program and the critical questions that should be investigated both in normal and altered gravity.

3.1 CENTRAL PROCESSING

3.1.1 Objectives

- Understand the central neural mechanisms that contribute to spatial orientation
- Understand how signals from multiple senses related to gaze, body orientation, and motion are integrated at various sites in the central nervous system
- Understand the central processing that leads to space motion sickness
- Understand the neural basis for the adaptive response to altered sensory environments
- Develop models of central processing that can be used as heuristic and productive tools for future experiments
- Implement pharmacological studies in order to provide a rational basis for developing drug therapies for space motion sickness
- Develop, test, and validate countermeasures for neurosensory aberrations caused by exposure to microgravity.

3.1.2 Critical Questions (In priority order)

1. Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?
2. What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum? Do thalamo-cortical systems play a role in generating this reference? What are the characteristics of the velocity storage system in relation to gravity?
3. What are the molecular signals that modulate or evoke motion sickness? Are these signals of neural (synaptic transmitters) or neuroendocrine (hormonall) origin? What changes in the release of these messengers can be correlated with space motion sickness?
4. What neuronal models can be used to understand central processing and adaptation in altered gravitational states?
5. At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?

6. How are receptors for anti-motion sickness drugs distributed within central vestibular and other pathways?

7. Does altered gravity lead to changes in neural control of biological rhythms, such as sleep and temperature?

8. What changes are produced in the visual system by altered states of gravity?

3.2 MOTOR

3.2.1 Objectives

1. Determine the characteristics of motor control of gaze, posture, and locomotion in altered gravity

2. Determine how sensory inputs and coordination of muscular actions are organized before, during, and after flight

3. Determine changes in oculomotor, somatomotor, and autonomic systems in microgravity

4. Understand the neural circuits and physiological signals controlling motion in three-dimensional space under normal conditions and in the context of adaptation to altered gravity.

3.2.2 Critical Questions (In priority order)

1. How does gaze stabilization change in altered gravitational states? What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?

2. How are sensory inputs and coordination of muscular activities organized for maintenance of posture and generation of locomotion before, during, and after flight?

3. What are the optimal procedures for readaptation to 1-g after adaptation to microgravity?

4. What are the neural pathways that control the autonomic and endocrine responses characteristic of motion sickness and what are the pharmacological and physiological properties of these pathways?

5. What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?

6. Does a change in otolithic and proprioceptive activity play a role in regulating calcium or antigravity muscle growth and function during development and aging or exposure to altered gravitational states?

7. What models of sensory-motor transformation can be used to most accurately predict motor behavior in altered gravitational states?

8. How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?

3.3 COGNITIVE/SPATIAL ORIENTATION

3.3.1 Objectives

- Understand how adaptive changes in the vestibular, proprioceptive, somatosensory and visual systems lead to changes in spatial orientation

- Determine the perceptual processes, neurophysiological mechanisms, and cortical structures underlying the perception of space and self and surround motion

- Determine the changes that occur in central nervous system activity during the process of adaptation to altered gravitational conditions.

3.3.2 Critical Questions (In priority order)

1. What are the psychophysical correlates and neural basis for perception of motion?

2. What psychophysical correlates can best be used to describe spatial orientation? What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?

3. Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?

4. What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?

5. What processes explain the altered perceptions of joint and body position in microgravity?

6. What perceptual and performance changes are produced by drugs used in the treatment of motion sickness?

3.4 SENSORY RECEPTORS

3.4.1 Objective

- Understand the effect of different gravitational environments on the structure and function of sensory receptors.

3.4.2 Critical Questions (In priority order)

1. What are the structure-function relationships of the otolith organs and semicircular canals, including development, plasticity, and degeneration?

2. What are the relevant sensors for posture, body movement, and spatial orientation, including the transduction process?

3. What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?

4.0 TECHNOLOGY

Table 1 summarizes major areas of research in neuroscience and the space-flight eras for which each area is important.

Table 1

SUMMARY OF REQUIREMENTS FOR NEUROSCIENCE RESEARCH BY SPACEFLIGHT ERA

Major Areas of Research	Ground Based	STS	Early SSF	SSF (PMC)
Processing of signals from the canals and otoliths	X	X		X
Neural basis of 3-D orientation	X	X		X
Neural and neuroendocrine basis for motion sickness	X	X		X
Central processing and adaptation to microgravity	X	X	X	X
Develop training programs and devices for pre-adaptation to microgravity	X	X	X	X
Neuronal models of adaptation to microgravity	X	X		X
Characteristics of motor control of posture and locomotion — before, during, and after flight	X	X	X	X
Psychophysical studies of spatial orientation	X	X		X
Multisensory interactions of vestibular, visual and auditory inputs	X	X		X
Effects of different gravitational environments on the structure and function of sensory receptors	X	X		X
Structure-function relationships of the otolith organs and canals, including development, plasticity and degeneration	X	X		X

There is a critical need to develop or utilize a series of instruments and stimulation and recording techniques for the neuroscience research needed to accomplish the goals and objectives and answer the questions listed in this plan. In some cases, the technology is available; however, it may need modification to meet NASA's flight requirements. In a number of areas, new technology or facilities must be developed. A table of technology and facilities that are important to ground-based and/or flight research in the neurosciences is listed below.

Table 2

TECHNOLOGY/FACILITY REQUIREMENTS

		Priority+	
		Develop New Technology	Existing Technology
1.	Eye Movement Recording Processing (R)	1	
2.	Noninvasive EMG Recording (R)	1	
3.	Linear Sled/Rotation Devices (S)		1
4.	Simulation Devices for Pre-adaptation to Microgravity, e.g., PAT, Dry Immersion (S)		1
5.	3-D Body Movement Recording (R)		2
6.	Visual Environment Stimulator (S)	2	
7.	Neural Modeling Software/Hardware (T)	2	
8.	Motor System Work Station (Flight Qualified) (S/R)		2
9.	Noninvasive Neural Recording:EEG, Magnetic (R)	3*	
10.	Magnetic Resonance Imaging and Spectroscopy (R)		3
11.	Organized Cell and Organ Cultures (S/R)		3
12.	Micro Drug Delivery & Bioassay (S/R)		4
13.	Infrared Imaging (R)		4
14.	Telepresence & Robotics (T)	4	
15.	3-D Morphological Reconstruction (T)	5	
16.	Vestibular Prostheses (S/R)	5	

+Priority 1-5 (1-Highest, 5-Lowest)

S-Stimulating
R-Recording
T-Technique
*Interagency Effort

5.0 RESEARCH STRATEGY

The neuroscience research area priorities for each of the NASA mission eras are presented in Table 3.

Table 3

NEUROSCIENCE DISCIPLINE RANKINGS

AREAS	STS ERA CURRENT 1992-1995	SPACE STATION ERA 1991-2000	SPACE EXPLORATION ERA 2000-3000
CENTRAL PROCESSING	3	3	3
MOTOR SYSTEMS	2	1	1
COGNITIVE/SPATIAL ORIENTATION	1	2	2
SENSORY	4	4	4

Future research in the neurosciences will need to expand into new areas as NASA plans longer duration missions. Ground-based research will have to explore new models for simulating microgravity and new techniques for collecting and analyzing data. Major research emphasis should continue to be placed on obtaining an understanding of the acute changes that occur during the first few days of space flight. Flight experiments should be designed to obtain measures early in flight on all crewmembers using the same techniques. Where possible, multisensory experiments should be developed in order to study changes in spatial orientation.

As one part of its participation in the Federal activities of the Decade of the Brain, NASA plans to fly a Spacelab mission dedicated to research in the brain and behavioral sciences, which is called "Neurolab". NASA is proposing a four-part program as its contribution to the Decade of the Brain. This program will include a Spacelab flight dedicated to neuroscience research; a number of centers, which will be part of the NASA Specialized Centers of Research and Training (NSCORT) Program; individual investigators; and enhanced use of NASA's specialized research resources by investigators. NASA has submitted a draft plan for its participation in the Federal program and this plan details the proposed areas of research in the neurosciences. It was the consensus of the Neuroscience Discipline Working Group that a dedicated space flight in the areas of brain and behavioral sciences would greatly enhance NASA's ground-based and flight research program and provide unique opportunities for the neuroscience community.

5.1 VESTIBULO-OCULAR REFLEX (VOR) AND VISUAL-VESTIBULO-OCULAR REFLEX (VVOR)

In order to determine whether there are changes in the angular and linear VOR that compromise stabilization of gaze and correlate with space motion sickness or adaptation to microgravity, magnetic eye-coil recordings or video recording of eye positions should be used with human subjects in both ground-based and inflight studies. (The inability to record true eye position, and errors in gain and phase measures associated with electro-oculography, have handicapped previous investigations and will continue to be a problem in the immediate future.) Video techniques for measurement of torsional eye movements should be developed. Studies of saccadic eye movements in response to visual targets should be conducted using sophisticated analysis techniques in order to determine whether changes in saccadic system parameters occur in microgravity.

The linear VOR should be characterized in humans, as it has been in nonhuman primates. It is important that NASA complete the air-bearing linear accelerator device at the Vestibular Research Facility at Ames Research Center. Engineering evaluation studies should be initiated to explore the feasibility of a gimbaled restraint system that would allow humans to be stimulated in different planes. Consideration should also be given to the development of a three-dimensional "ganzfeld" to surround the subject, in order to study visual-vestibular interactions in response to linear acceleration. Again, magnetic eye coil recording or video recording capability must be available to accurately record eye position. Ideally, all astronauts who fly in space and are available for testing should be tested on the linear accelerator as soon as possible after flight to develop a data base for understanding changes in the linear VOR in space. Their ocular responses should also be correlated with their history of space motion sickness symptom development during adaptation to space.

It has been hypothesized that an asymmetry in otoconial mass may be a factor in the development of space motion sickness, and some individuals show an asymmetry in ocular counterrolling when tested in microgravity. The possible role of central and peripheral asymmetries in the etiology of space motion sickness should be investigated. Such studies need to be conducted very early in flight, before changes are masked by adaptation.

There is evidence from Soviet studies that water or dry immersion leads to changes in vestibulo-oculomotor reflexes and in posture similar to those seen in weightlessness. There is also anecdotal evidence that astronauts who spend time working in the neutral buoyancy tank appear to adapt better to microgravity. Therefore, a pilot study to evaluate this possibility is warranted.

5.2 SPATIAL ORIENTATION

Historically, studies of spatial orientation have evaluated sensory and motor function using static tests in single dimensions. Although there have been many tests of visual-vestibular interactions, these are typically performed about a single axis. It is obvious that normal orientation is a function of multiple inputs, such as vision, audition, vestibular, proprioceptive-somatosensory, and cognitive, generated in a three-

dimensional dynamic environment with gravity as a constant background reference. Self-movement or movement of the visual surround may play an important role in generating cues for spatial orientation and should be investigated. Recent engineering research efforts (NASA-Ames Research Center; U.S. Air Force-Wright Patterson AFB) have led to the development of a number of simulation devices that can generate three-dimensional sound and virtual image displays. Such devices can be incorporated into tests of spatial orientation during exposure to microgravity.

5.3 POSTURAL AND NEUROMUSCULAR CONTROL MECHANISMS

Changes in central control mechanisms related to posture and the effects of microgravity should be understood. Computer analysis of gait before and after flight should be conducted, evaluating both translational and postural competence as well as stabilization of gaze. Studies using animal models should be implemented wherever practical to investigate the role of central mechanisms in muscle atrophy and changes in neuromuscular activation patterns as a result of prolonged exposure to microgravity.

5.4 SPACE MOTION SICKNESS

At the present time, the etiology of space motion sickness and its impact on performance are not clearly understood. Attempts to determine the correlates of space motion sickness have centered on the use of conventional, ground-based tests of vestibular and perceptual-motor function.

The critical research questions related to space motion sickness remain the same for short-duration missions. Long-duration missions employing artificial gravity will raise new questions, which are addressed in the section related to artificial gravity.

It has not been possible to identify crewmembers who will be susceptible to space motion sickness using ground-based measurements and parabolic flight tests. Alternative research strategies involving the use of animal models and other appropriate experiments involving humans must be developed and pursued. As a first step, a workshop addressing alternate strategies for the investigation of space motion sickness should be conducted. The product of the workshop would be a short- and long-term plan to investigate the etiology of the disorder and the development of prophylaxis and therapy. As mentioned above, NASA Life Sciences is developing a number of preflight adaptation devices that may adapt astronauts to the visual-vestibular stimulus conflict, presumed to occur at the outset of exposure to microgravity.

5.5 CENTRAL NERVOUS SYSTEM STRUCTURE AND FUNCTION

Before the Space Exploration Initiative (SEI) is implemented, it will be necessary for NASA to develop programs directed at evaluating the effects of long-duration space flight on the central nervous system. In addition, countermeasures such as "artificial gravity" will require detailed studies of neurosensory adaptation to unusual environments. Issues to be addressed for SEI are:

- Do long-duration missions and the subsequent decrease in afferent information to the vestibular, proprioceptive and somatosensory systems result in morphological changes in mechanoreceptors; are these changes prevented and/or reversed by artificial gravity?

- Does physiological deafferentation (sensory deprivation) lead to changes in neuronal networks that are slowly or not reversed and, therefore, compromise function upon return to Earth's gravity and what is the rate of readaptation?

- Can humans adapt to continuous rotation or intermittent centrifugation during long-duration missions?

In order to address these questions it will be necessary to develop research programs in the neurosciences to study neurosensory changes that occur in complex acceleration environments. These programs should be integrated with studies of behavior and performance related to exposure to artificial gravity.

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PHYSIOLOGICAL CHANGES ASSOCIATED WITH SHORT-TERM AND LONG-TERM SPACE FLIGHT

Physiological Parameter	Short-Term Space Flights[a] (1–14 days)	Long-Term Space Flights (more than 2 weeks)[b]	
		Pre- vs. Inflight	Pre- vs. Postflight
Cardiopulmonary System			
Heart rate (resting)	Slight increase inflight. Increased postflight; peaks during launch and reentry, normal or slightly increased during mission. RPB[c]: up to one week.	Normal or slightly increased.	Increased. RPB[c]: 3 weeks.
Blood pressure (resting)	Normal; decreased postflight.	Diastolic blood pressure reduced.	Decreased mean arterial pressure.
Orthostatic tolerance	Decreased after flights longer than 5 hours. Exaggerated cardiovascular responses to tilt test, stand test, and LBNP postflight. RPB[c]: 3–14 days.	Highly exaggerated cardiovascular responses to inflight LBNP (especially during first 2 weeks), sometimes resulting in presyncope. Last inflight test comparable to R + O[d] (recovery day) test.	Exaggerated cardiovascular responses to LBNP. RPB[c]: up to 3 weeks.
Cardiac size	Normal or slightly decreased cardio/thoracic ratio (C/T) postflight.		C/T ratio decreased postflight.
Stroke volume	Increased the first 24 hours inflight, then decreased by 15%.	Same as short duration missions.	12% decrease on average.
Left end diastolic volume	Same as stroke volume.	Same as short duration missions.	16% decrease on average.
Cardiac output	Unchanged.	Unchanged.	Variable RPB[c]: 3–4 weeks.
Central venous pressure (indirect measurement)	Gradual decrease over 7 days inflight.	Not measured.	Not measured.
Left cardiac muscle mass thickness	Unchanged.	Unchanged.	11% decrease, return to normal after 3 weeks.
Cardiac electrical activity (ECG/VCG)	Moderate rightward shift in QRS and T postflight.	Increased PR interval, QT_c interval, and QRS vector magnitude.	Slight increase in QRS duration and magnitude; increase in PR interval duration.
Arrhythmias	Usually premature atrial and ventricular beats (PABs, PVBs). Isolated cases of nodal tachycardia, ectopic beats, and supraventricular bigeminy inflight.	PVBs and occasional PABs; sinus or nodal arrhythmia at release of LBNP inflight.	Occasional unifocal PABs and PVBs.

PHYSIOLOGICAL CHANGES ASSOCIATED WITH SHORT-TERM AND LONG-TERM SPACE FLIGHT

Physiological Parameter	Short-Term Space Flights[a] (1–14 days)	Long-Term Space Flights (more than 2 weeks)[b]	
		Pre- vs. Inflight	Pre- vs. Postflight
Systolic time intervals	Not measured.	Not measured.	Increase in resting and LBNP-stressed PEP/ET Ratio. RPB[c]: 2 weeks.
Exercise capacity	No change or decreased postflight; increased HR for same O_2 consumption; no change in efficiency. RPB[c]: 3–8 days.	Submaximal exercise capacity unchanged.	Decreased postflight, recovery time inversely related to amount of inflight exercise, rather than mission duration.
Lung volume	Not measured.	Vital capacity decreased 10%.	No change.
Leg volume	Decreased up to 3% postflight. Inflight, leg volume decreases exponentially during first 24 hours, and plateaus within 3 to 5 days.	Same as short missions.	15% decrease in calf circumference.
Leg blood flow	Not measured.	Marked increase.	Normal or slightly increased.
Venous compliance in legs	Not measured.	Increased: continues to increase for 10 days or more; slow decrease later inflight.	Normal or slightly increased.
Body Fluids			
Total body water	3% decrease inflight.		Decreased postflight.
Plasma volume	Decreased postflight (except Gemini 7 and 8).		Markedly decreased postflight. RPB: 2 weeks increased at R + 0; decreased R + 2 (hydration effect).
Hematocrit	Slightly increased postflight.		
Hemoglobin	Normal or slightly increased postflight.	Increased first inflight sample; slowly declines later inflight.	Decreased postflight RPB: 1–2 months.
Red blood cell (RBC) mass	Decreased postflight; RPB: at least 2 weeks.	Decreased ~15% during first 2–3 weeks inflight; begins to recover after about 60 days; recovery of RBC mass is independent of the stay time in space.	Decreased postflight RPB: 2 weeks to 3 months following landing.
Red cell half-life (^{51}Cr)	No change.		No change.

Iron turnover			No change.
Mean corpuscular volume (MCV)	Increased postflight; RPB: at least 2 weeks.		Variable, but within normal limits.
Mean corpuscular hemoglobin (MCH)	Increased postflight; RPB: 2 weeks.		Variable, but within normal limits.
Mean corpuscular hemoglobin concentration (MCHC)	Increased postflight; RPB: at least 2 weeks.		Variable, but within normal limits.
Reticulocytes	Decreased postflight; RPB: 1 week.		Decreased postflight. In Skylab, RPB: 2–3 weeks for 28-day mission, 1 week for 59-day mission, and 1 day for 84-day mission.
White blood cells	Increased postflight, especially neutrophils; lymphocytes decreased; RPB: 1–2 days. No significant changes in the T/B lymphocyte ratios.		Increased, especially neutrophils; postflight reduction in number of T-cells and reduced T-cell function as measured by PHA* responsiveness; RPB: 3–7 days; transient postflight elevation in B-cells; RPB: 3 days.
Red blood cell morphology	No significant changes observed postflight.	Increase in percentage of echinocytes; decrease in discocytes.	Rapid reversal of inflight changes in distribution of red cell shapes; significantly increased potassium influx; RPB: 3 days.
Plasma proteins	Occasional postflight elevations in $\alpha 2$-Globulin, due to increases of haptoglobin, ceruloplasmin, and $\alpha 2$-Macroglobulin; elevated IgA and C_3 factor.		No significant changes.
Red cell enzymes	No consistent postflight changes.	Decrease in phosphofructokinase; no evidence of lipid peroxidation and red blood cell damage.	No consistent postflight changes.
Serum/plasma electrolytes	Decreased K and Mg postflight.	Decreased Na, Cl, and osmolality; slight increase in K and PO_4.	Postflight decreases in Na, K, Cl, Mg; increase in PO_4 and osmolality.
Serum/plasma hormones	Inflight increases in ADH, ANF, and decreases in ACTH, aldosterone and cortisol. Inflight decrease in glucose.	Increases in cortisol. Decreases in ACTH, insulin.	Postflight increases in angiotensin, aldosterone, thyroxine, TSH and GH; decrease in ACTH.

PHYSIOLOGICAL CHANGES ASSOCIATED WITH SHORT-TERM AND LONG-TERM SPACE FLIGHT

Physiological Parameter	Short-Term Space Flights[a] (1–14 days)	Long-Term Space Flights (more than 2 weeks)[b]	
		Pre- vs. Inflight	Pre- vs. Postflight
Serum/plasma metabolites & enzymes	Postflight increases in blood urea nitrogen, creatinine, and glucose; decreases in lactic acid dehydrogenase, creatinine phosphokinase, albumin, triglycerides, cholesterol, and uric acid.		Postflight decrease in cholesterol, uric acid.
Urine volume	Decreased postflight.	Decreased early inflight.	Decreased postflight.
Urine electrolytes	Postflight increases in Ca, creatinine, PO_4, and osmolality. Decreases in Na, K, Cl, Mg.	Increased osmolality, Na, K, Cl, Mg, Ca, PO_4. Decrease in uric acid excretion.	Increase in Ca excretion; initial postflight decreases in Na, K, Cl, Mg, PO_4, uric acid; Na and Cl excretion increased in 2nd and 3rd week postflight.
Urinary hormones	Inflight decreases in 17-OH-corticosteroids, increase in aldosterone; postflight increases in cortisol, aldosterone, ADH, and pregnanediol; decreases in epinephrine, 17-OH-corticosteroids, androsterone, and etiocholanolone.	Inflight increases in cortisol, aldosterone, and total 17-ketosteroids; decrease in ADH.	Increase in cortisol, aldosterone, norepinephrine; decrease in total 17-OH-corticosteroids, ADH.
Urinary amino acids	Postflight increases in taurine and β-alanine; decreases in glycine, alanine, and tyrosine.	Increased inflight.	Increased postflight.
Sensory Systems			
Audition	No change in thresholds postflight.		No change in thresholds postflight.
Gustation & olfaction	Subjective and varied human experience. No impairments noted.	Same as shorter missions.	Same as shorter missions.
Somatosensory	Subjective and varied human experience. No impairments noted.	Subjective experiences (e.g., tingling of feet).	

Vision	Transitory postflight decrease in intraocular tension; postflight decreases in visual field; constriction of blood vessels in retina observed postflight; dark adapted crews reported light flashes with eyes open or closed; possible postflight changes in color vision. Decrease in visual motor task performance and contrast discrimination. No change in inflight contrast discrimination, or distant and near visual acuity.	Light flashes reported by dark adapted subjects frequency related to latitude (highest in South Atlantic Anomaly, lowest over poles).	No significant changes except for transient decreases in intraocular pressures.
Vestibular system	40–50% of astronauts/cosmonauts exhibit inflight neurovestibular effects including immediate reflex motor responses (postural illusions, sensations of tumbling or rotation, nystagmus, dizziness, vertigo) and space motion sickness (pallor, cold sweating, nausea, vomiting). Motion sickness symptoms appear early inflight, and subside or disappear in 2–7 days. Postflight difficulties in postural equilibrium with eyes closed, or other vestibular disturbances.	Inflight vestibular disturbances are same as for shorter missions; markedly decreased susceptibility to provocative motion stimuli (cross-coupled angular acceleration) after 2–7 days adaptation period. Cosmonauts have reported occasional reappearance of illusions during long-duration missions.	Immunity to provocative motion continues for several days postflight. Marked postflight disturbances in postural equilibrium with eyes closed. Some cosmonauts exhibited additional vestibular disturbances postflight, including dizziness, nausea, and vomiting.
Musculoskeletal system			
Height	Slight increase during first week inflight (~1.3 cm). RPB: 1 day.	Increased during first 2 weeks inflight (maximum 3–6 cm); stabilizes thereafter.	Height returns to normal on R + 0.
Mass	Postflight weight losses, average about 3.4%; about 2/3 of the loss is due to water loss, the remainder due to loss of lean body mass and fat.	Inflight weight losses average 3–4% during first 5 days; thereafter, weight gradually declines for the remainder of the mission. Early inflight losses are probably mainly due to loss of fluids; later losses are metabolic.	Rapid weight gain during first 5 days postflight, mainly due to replenishment of fluids. Slower weight gain from R + 5** to R + 2 or 3 weeks. Amount of postflight weight loss is inversely related to inflight caloric intake.

PHYSIOLOGICAL CHANGES ASSOCIATED WITH SHORT-TERM AND LONG-TERM SPACE FLIGHT

Physiological Parameter	Short-Term Space Flights[a] (1–14 days)	Long-Term Space Flights (more than 2 weeks)[b]	
		Pre- vs. Inflight	Pre- vs. Postflight
Body composition		Fat is probably replacing muscle tissue. Muscle mass, depending on exercise regimens, is partially preserved.	
Total body volume	Decreased postflight.	Center of mass shifts headward.	Decreased postflight.
Limb volume	Inflight leg volume decreases exponentially during first mission day; thereafter, rate of decrease declines until reaching a plateau within 3–5 days. Postflight decrements in leg volume up to 3%; rapid increase immediately postflight, followed by slower RPB.	Early inflight period same as short missions. Leg volume may continue to decrease slightly throughout mission. Arm volume decreases slightly.	Rapid increase in leg volume immediately postflight, followed by slower RPB.
Muscle strength	Decreased inflight and postflight; RPB: 1–2 weeks.		Postflight decrease in leg muscle strength, particularly extensors. Increased use of inflight exercise appears to reduce postflight strength losses, regardless of mission duration. Arm strength is normal or slightly decreased postflight.
EMG analysis	Postflight EMGs from gastrocnemius suggest increased susceptibility to fatigue and reduced muscular efficiency. EMGs from arm muscles show no change.		Postflight EMGs from gastrocnemius show shift to higher frequencies, suggesting deterioration of muscle tissue; EMGs indicate increased susceptibility to fatigue. RPB: about 4 days.
Reflexes (Achilles tendon)	Reflex duration decreased postflight.		Reflex duration decreased postflight (by 30% or more). Reflex magnitude increased. Compensatory increase in reflex duration about 2 weeks postflight; RPB: about 1 month.

Nitrogen & phosphorus balance		Negative balances early inflight; less negative or slightly positive balances later inflight.	Rapid return to markedly positive balances postflight.
Bone density	Os calcis density decreased postflight. Radius and ulna show variable changes, depending upon method used to measure density.		Os calcis density decreased postflight; amount of loss is correlated with mission duration. Little or no loss from non-weightbearing bones. RPB is gradual; recovery time is about the same as mission duration.
Calcium balance	Increasing negative calcium balance inflight.	Excretion of Ca in urine increases during 1st month inflight, then plateaus. Fecal Ca excretion declines until day 10, then increases continually throughout flight. Ca balance is positive preflight, becoming increasingly negative throughout flight.	Urine Ca content drops below preflight baselines by day 10; fecal Ca content declines, but does not reach preflight baseline by day 20. Markedly negative Ca balance postflight, becoming much less negative by day 10. Ca balance still slightly negative on day 20. RPB: at least several weeks.

[a] Compiled from biomedical data collected during the following space programs: Mercury, Gemini, Apollo, ASTP, Vostok, Voskhod, Soyuz and Shuttle Spacelab.
[b] Compiled from biomedical data collected during Skylab and Salyut missions.
[c] RPB: Return to preflight baseline.